RECEIVED
CENTRAL FAX CENTER
DEC 27 2006

REMARKS

This is in response to the Office Action mailed on September 27. Claims 1-35 are pending in the application. In the Office Action, claims 1-35 were rejected. No amendments have been made to the claims.

The Office Action rejected claims 1-35 under 35 U.S.C. §103(a) as being unpatentable over Carlyle et al. International Publication No. WO 99/37337 (the Carlyle application) in view of U.S. Patent No. 6,124,131 (the Semenza patent) or Tsuzuki et al. (the Cancer Research Article). The Office Action alleges that the Carlyle application teaches a medical device on to which VEGF has been attached to promote population of the device with viable cells and other positive results. The Office Action further alleges that the Carlyle application teaches all the claimed devices in detail through the reference and also details means for attaching the peptide to the device in all of the methods Applicants claim. The Office Action further alleges that the Carlyle application teaches all of the claimed limitations except that the reference uses VEGF and does not teach using a VEGF stimulation compound. The Office Action then alleges that at the time that the invention was made, it would have been obvious to one of ordinary skill in the art to substitute a known VEGF stimulation compound for the VEGF used by the Carlyle application because such a compound would have caused the production of a desired compound VEGF.

The Office Action admits that the Carlyle application does not teach using HIF-1α as the stimulator/agonist of VEGF. However, the Office Action alleges that it would have been obvious at the time the invention was made to use HIF-1α in lieu of VEGF in the process disclosed in the Carlyle application or device disclosed in the Carlyle application because the Semenza patent and Cancer Research Article teach that HIF-1α is a known stimulator of VEGF.

Applicants respectfully disagree that claim 1 is made obvious by the Carlyle application in view of either the Semenza patent or the Cancer Research Article because there is no teaching or suggestion to combine the references. Elements of claim 1 include a medical device comprising a stimulation compound associated with the medical device wherein the stimulation compounds stimulates production of VEGF, the medical device being an implantable medical device, a catheter, a dressing or a surgical instrument.

There is no teaching or suggestion in any of the cited references of a medical device having a stimulation compound associated therewith where the stimulation compounds stimulates production of VEGF. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The Office Action has not provided any teaching or suggestion in any of the references to make the combination. Therefore, the combination of references is improper.

The Office Action states that one cannot show non-obviousness by attacking references individually where the rejections are based upon a combination of references. *In re* Keller, 642 F.2d 413, 208 USPQ (CCPA 1981); *In re* Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants submit that the references are not being individually attacked as alleged. Rather, Applicants submit that the combination of references is improper. To combine references, there must be some teaching or suggestion to make the combination that is not based upon Applicants' disclosure. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). There are three possible sources for motivation to combine references: the nature of the problem to be solved, the teaching of the prior art, and the knowledge of the persons of ordinary skill in the art. *In re Rousset*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). Absent the present invention, there is no teaching or suggestion to combine the Carlyle Application with either the Semenza Patent or the Cancer Research Article.

The Carlyle Application addresses issues relating to biocompatibility of an implanted prosthesis. The Semenza Patent addresses the discovery of HIF-1α as VEGF promoter. The Cancer Research Article addresses the effect of HIF-1α on the production of VEGF and the effect of VEGF on the growth rate of tumors. There is no teaching or suggestion in the Carlyle Application of using HIF-1α as a stimulation compound for the production of VEGF on a medical device. Similarly, there is no teaching or suggestion in either the Semenza Patent or the Cancer Research Article of utilizing HIF-1α on a medical device. Therefore, there is no teaching or suggestion absent the present invention for making the combination of references. Therefore, the combination of references is improper.

Applicants would also like to address the allegation in the Office Action that the coating of a VEGF stimulating compound on a medical device would produce the same desired results sought by Carlyle. Applicants acknowledge the Carlyle Application at page 25, ll. 18-22. However, Applicants believed and still believe that the claimed medical device in claim 1 was sufficiently different from the disclosure of the Carlyle Patent and provided advantages over the Carlyle Patent such that the claimed invention was not obvious over the Carlyle Patent. The Office Action failed to address the numerous passages provided in the previous Response that illustrate how different results are obtained.

Specifically, the specification discloses several reasons or advantages of utilizing a stimulation compound to produce VEGF as compared to coating a medical device with VEGF. For instance, the reasons or advantages include, but are not limited to:

> The HIF and/or other stimulation compounds direct natural processes that encourage cellular activity and vascularization near the medical device without the effort associated with in vitro manipulation of cells.

Page 5, lines 19-21.

> Incorporation of a stimulation molecule capable of stimulating VEGF production near the surface of a medical device, such as a heart valve prosthesis, or a portion thereof, could reduce the risk of thrombosis and the long-term need for anticoagulation therapy.

Page 6, lines 2-5.

> The stimulation compound generally is releasably associated with the biocompatible material such that the stimulation compound is gradually released into the fluids and/or tissue surrounding the medical device.

Page 18, lines 8-10.

> While the stimulation compound stimulates the generation of VEGF in the vicinity of the biocompatible material, it may be desirable to also have VEGF associated with the biocompatible material. ... Thus, the combined use of an associated stimulation compound and associated VEGF can have a synergistic effect with respect to promoting the colonization of the biocompatible material.

Page 25, lines 5-7, 13-15.

> In other embodiments, a portion of biocompatible material with associated stimulation compounds is placed in a cell culture system as a time release agent to gradually release stimulation compound into the cell culture. Stimulation compound could be desirable in the cell culture system to provide a constant regeneration of VEGF through cellular activity.

Page 28, line 30 – page 29, line 2.

Therefore, associating a stimulation compound with a medical device to produce VEGF clearly does not produce the same results as coating a medical device with VEGF. For the foregoing reasons, claim 1 is believed to be in allowable form. Reconsideration and allowance of claim 1 are respectfully requested.

Claims 2-30 depend from independent claim 1 and were rejected for the reasons stated with respect to claim 1. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 1. Reconsideration and allowance of claims 2-30 are respectfully requested.

The Office Action also rejected independent claim 31 as being obvious for the reasons stated with respect to claim 1. For the reasons stated with respect to claim 1, claim 31 is not obvious and also is in allowable form. Reconsideration and allowance of claim 31 are respectfully requested.

Claims 32-35 depend from independent claim 31 and were rejected for the reasons stated with respect to claim 31. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 31. Reconsideration and allowance of claims 32-35 are respectfully requested.

The Director is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

WESTMAN, CHAMPLIN & KELLY, P.A.

By: _____

Peter J. Iris, Reg. No. 48,774
Suite 1400
900 Second Avenue South
Minneapolis, Minnesota 55402-3319
Phone: (612) 334-3222 Fax: (612) 334-3312

PJI:tlr